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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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- Published:**
- *with international search report*
 - *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*
- (88) Date of publication of the international search report:
19 August 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **METHOD FOR REFOLDING NEISSERIAL NSPA PROTEIN**

(57) Abstract: The present invention provides an isolated refolded NspA protein, and a method of preparing it.

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INTERNATIONAL SEARCH REPORT

International Application No

P 03/10085

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/22 A61K39/095

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JANSEN C ET AL: "Biochemical and biophysical characterization of in vitro folded outer membrane porin PorA of Neisseria meningitidis" BIOCHIMICA ET BIOPHYSICA ACTA. BIOMEMBRANES, AMSTERDAM, NL, vol. 1464, no. 2, 5 April 2000 (2000-04-05), pages 284-298, XP004273195 ISSN: 0005-2736	11
Y	page 285, column 1, paragraph 2 page 285, column 2, last paragraph - page 286 ----- -/--	1-10, 12-36

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- *G* document member of the same patent family

Date of the actual completion of the international search

2 June 2004

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/10085

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>WO 96/29412 A (BRODEUR BERNARD R ;HAMEL JOSEE (CA); RIOUX CLEMENT (CA); IAF BIO V) 26 September 1996 (1996-09-26) cited in the application abstract page 1, line 5 - line 21 page 5, line 24 - page 6, line 12 page 15, line 19 - page 16, line 9 page 21, line 14 - line 33 page 22, line 10 - page 23, line 24 examples 4-6,8,12</p>	1-10, 12-17, 24-36
Y	<p>WO 00/71725 A (PIZZA MARIAGRAZIA ;RAPPUOLI RINO (IT); CHIRON SPA (IT); GIULIANI M) 30 November 2000 (2000-11-30) page 54, line 31 - page 55, line 16 claim 8; example 11</p>	18-21
Y	<p>KRAMER R A ET AL: "In vitro folding, purification and characterization of Escherichia coli outer membrane protease OmpT" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 267, no. 3, February 2000 (2000-02), pages 885-893, XP001189705 ISSN: 0014-2956 abstract page 886, column 1, paragraph 3</p>	8,9
Y	<p>DEKKER NIEK ET AL: "In vitro folding of Escherichia coli outer-membrane phospholipase A" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 232, no. 1, 1995, pages 214-219, XP008029422 ISSN: 0014-2956 page 214, column 2, last paragraph - page 215, column 1, paragraph 1</p>	8,9
Y	<p>WO 01/72337 A (GORRINGE ANDREW RICHARD ;HUDSON MICHAEL JOHN (GB); MICROBIOLOGICAL) 4 October 2001 (2001-10-04) page 3, line 25 - page 4, line 3 page 4, line 34 - page 5, line 4 page 10, line 19 - page 11, line 26</p>	22,23
Y	<p>WO 01/09350 A (DALEMANS WILFRIED L J ;SMITHKLINE BEECHAM BIOLOG (BE); THIRY GEORG) 8 February 2001 (2001-02-08) page 31, line 1 - line 11 page 36, line 5 - page 37, line 6</p>	18-23
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/10085

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MOE G R ET AL: "Differences in surface expression of NspA among Neisseria meningitidis group B strains" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, US, vol. 67, no. 11, November 1999 (1999-11), pages 5664-5675, XP002266209 ISSN: 0019-9567 abstract</p>	
P,X	<p>-----</p> <p>VANDEPUTTE-RUTTEN LUCY ET AL: "Crystal structure of neisserial surface protein A (NspA), a conserved outer membrane protein with vaccine potential." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 27, 4 July 2003 (2003-07-04), pages 24825-24830, XP002274972 ISSN: 0021-9258 abstract page 24825, column 2, last paragraph - page 24826, column 1, paragraph 1 page 24827, column 1, paragraph 1 page 24829, column 2, paragraph 2</p> <p>-----</p>	<p>1-5, 10-16</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/10085

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 26-28 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/10085

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9629412	A	26-09-1996	AP 1027 A	23-11-2001
			AU 716225 B2	24-02-2000
			AU 4934396 A	08-10-1996
			BR 9607651 A	17-11-1998
			CA 2215161 A1	26-09-1996
			WO 9629412 A1	26-09-1996
			CZ 9702914 A3	14-01-1998
			EA 1789 B1	27-08-2001
			EP 0815234 A1	07-01-1998
			HU 9702387 A2	28-05-1998
			JP 11500624 T	19-01-1999
			JP 2003189879 A	08-07-2003
			NO 974264 A	13-11-1997
			NZ 303118 A	28-07-2000
			OA 10742 A	10-12-2002
			PL 322363 A1	19-01-1998
			RO 117924 B	30-09-2002
			SI 9620035 A	31-12-1998
			SK 125597 A3	03-06-1998
			TR 9700971 T1	21-04-1998
			US 6287574 B1	11-09-2001
			ZA 9602109 A	09-09-1997
			TW 520375 B	11-02-2003
WO 0071725	A	30-11-2000	AU 5097700 A	12-12-2000
			BR 0010721 A	11-06-2002
			CA 2373236 A1	30-11-2000
			CN 1362992 T	07-08-2002
			EP 1179072 A2	13-02-2002
			WO 0071725 A2	30-11-2000
			JP 2003500420 T	07-01-2003
			NZ 515935 A	30-01-2004
WO 0172337	A	04-10-2001	AU 4260201 A	08-10-2001
			CA 2403993 A1	04-10-2001
			EP 1267938 A1	02-01-2003
			WO 0172337 A1	04-10-2001
			JP 2003528157 T	24-09-2003
			US 2003082211 A1	01-05-2003
WO 0109350	A	08-02-2001	AU 770360 B2	19-02-2004
			AU 6833600 A	19-02-2001
			BR 0012974 A	07-05-2002
			CA 2380840 A1	08-02-2001
			CN 1377415 T	30-10-2002
			CZ 20020403 A3	15-05-2002
			WO 0109350 A2	08-02-2001
			EP 1208214 A2	29-05-2002
			HU 0203056 A2	28-12-2002
			JP 2003506049 T	18-02-2003
			NO 20020506 A	02-04-2002
			PL 353891 A1	15-12-2003
			TR 200200275 T2	21-05-2002
			TR 200202448 T2	21-01-2003